

Figure 1: INO-4800 Humoral and neutralizing response against SARS-CoV-2 variants

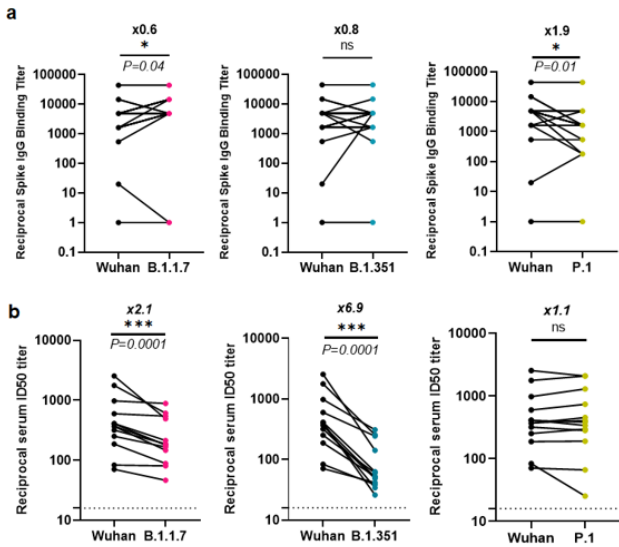
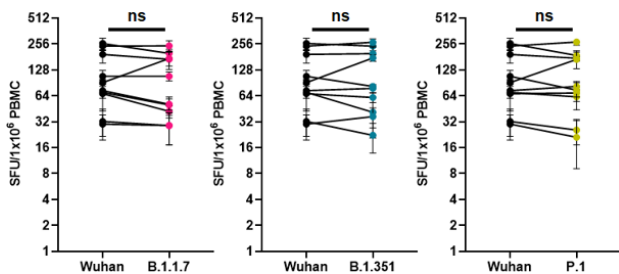


Figure 2: INO-4800 Cellular immune response against SARS-CoV-2 variants



Conclusion. INO-4800 vaccination induced neutralizing antibodies against all variants tested, with reduced levels detected against B.1.351. IFN γ T cell responses were fully maintained against all variants tested.

Disclosures. Viviane M. Andrade, PhD, Inovio Pharmaceuticals Inc. (Employee) Aaron Christensen-Quick, PhD, Inovio Pharmaceuticals, Inc (Employee) Joseph Agnes, PhD, Inovio (Employee, Shareholder) Jared Tur, PhD, Inovio (Employee) Charles C. Reed, PhD, Inovio Pharmaceuticals (Employee, Shareholder) Richa Kalia, MS, Inovio Pharmaceuticals (Employee, Other Financial or Material Support, I have stock options with Inovio Pharmaceuticals as an employee.) Idania Marrero, MD, PhD, Inovio Pharmaceuticals (Employee, Shareholder) Dustin Elwood, PhD, Inovio Pharmaceuticals (Employee) Katherine Schultheis, MSc, Inovio Pharmaceuticals (Employee) Emma Reuschel, PhD, Inovio Pharmaceuticals (Employee) Trevor McMullan, MSc, Inovio (Shareholder) Patrick Pezzoli, BS, Inovio (Employee) Kimberly A. Kraynyak, PhD, Inovio Pharmaceuticals (Employee, Other Financial or Material Support, Stock options) Albert Sylvester, MS, Inovio (Employee, Shareholder) Mammen P. Mammen Jr., MD, Inovio Pharmaceuticals (Employee) J Joseph Kim, PhD, Inovio (Employee) David Weiner, PhD, Inovio (Board Member, Grant/Research Support, Shareholder, I serve on the SAB in addition to the above activities) Trevor R. F. Smith, PhD, Inovio (Employee, Shareholder) Stephanie Ramos, PhD, Inovio Pharmaceuticals (Employee) Laurent Humeau, PhD, Inovio Pharmaceuticals (Employee) Jean Boyer, PhD, Inovio (Employee) Kate Broderick, PhD, Inovio (Employee)

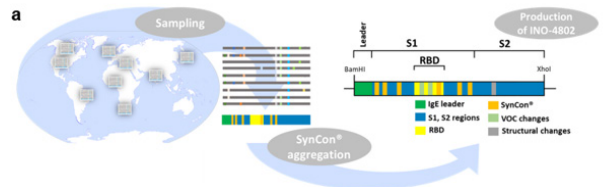
579. Design and Immunogenicity of a Pan-SARS-CoV-2 Synthetic DNA Vaccine
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Session: P-25. COVID-19 Vaccines

Background. First-generation COVID-19 vaccines are matched to spike protein of the Wuhan-H1 (WT) strain. Convalescent and vaccinee samples show reduced neutralization of SARS-CoV-2 variants of concern (VOC). Next generation DNA vaccines could be matched to single variants or synthetically designed for broader coverage of multiple VOCs.

Methods. The synthetic consensus (SynCon[®]) sequence for INO-4802 SARS-CoV-2 spike with focused RBD changes and dual proline mutations was codon-optimized (Figure 1). Sequences for wild-type (pWT) and B.1.351 (pB.1.351) were similarly optimized. Immunogenicity was evaluated in BALB/c mice. Pre-clinical efficacy was assessed in the Syrian Hamster model.

Figure 1. Design Strategy for INO-4802



Results. INO-4802 induced potent neutralizing antibody responses against WT, B.1.1.7, P.1, and B.1.351 VOC in a murine model. pWT vaccinated animals showed a 3-fold reduction in mean neutralizing ID50 for the B.1.351 pseudotyped virus. INO-4802 immunized animals had significantly higher ($p = 0.0408$) neutralizing capacity (mean ID50 816.16). ID50 of pB.1.351 serum was reduced 7-fold for B.1.1.7 and significantly lower ($p = 0.0068$) than INO-4802 (317.44). INO-4802 neutralized WT (548.28) comparable to pWT. INO-4802 also neutralized P.1 (1026.6) (Figure 2). pWT, pB.1.351 or INO-4802 induced similar T-cell responses against all variants. INO-4802 skewed towards a TH1-response. All hamsters vaccinated with INO-4802 or pB.1.351 were protected from weight loss after B.1.351 live virus challenge. 4/6 pWT immunized hamsters were completely protected. pWT immunized hamsters neutralized WT (1090) but not B.1.351 (39.16). INO-4802 neutralized both WT (672.2) and B.1.351 (1121) (Figure 3). We observed higher increase of binding titers following heterologous boost with INO-4802 ($3.6 - 4.4 \log_2$ -fold change) than homologous boost with pWT ($2.0 - 2.4 \log_2$ fold change) (Figure 4).

Figure 2. INO-4802 Induces Functional Humoral Immune Response Against SARS-CoV-2 Variants of Concern

Figure 2

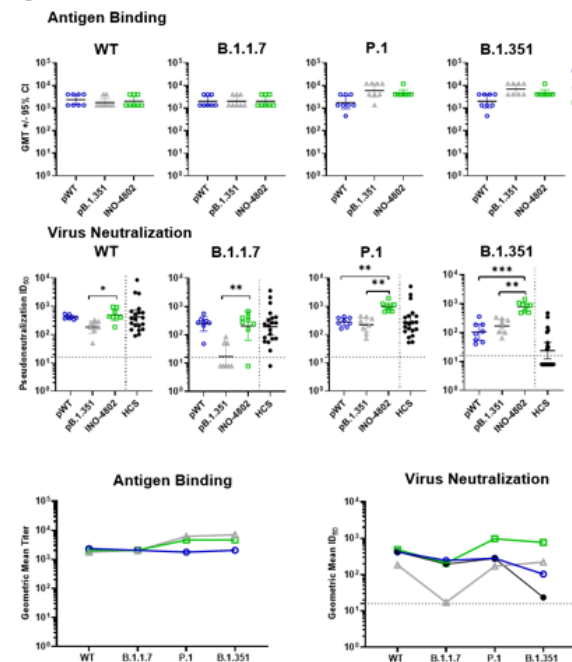


Figure 3. INO-4802 Protects Hamsters Against Challenge With B.1.351 Live Virus

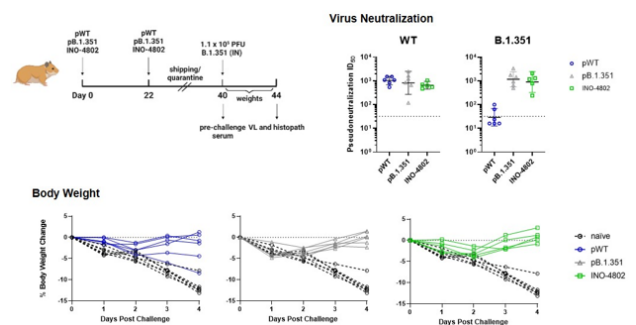
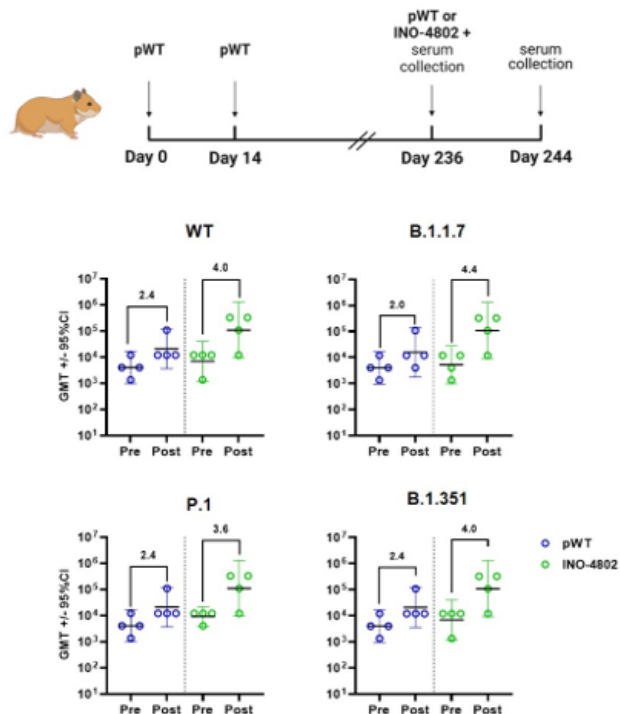


Figure 4. Heterologous Boost with INO-4802 Induces Humoral Immune Response Against SARS-CoV-2 Variants



Conclusion. Vaccines matching single VOCs, like pB.1.351 and pWT, elicit responses against the matched antigen but have reduced cross-reactivity. Presenting a pan-SARS-CoV-2 approach, INO-4802 may offer substantial advantages in terms of cross-strain protection, reduced susceptibility to escape mutants and non-restricted geographical use.

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580. Hesitancy in Uptake and Recommendation of COVID-19 Vaccines by US Healthcare Workers

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Session: P-25. COVID-19 Vaccines

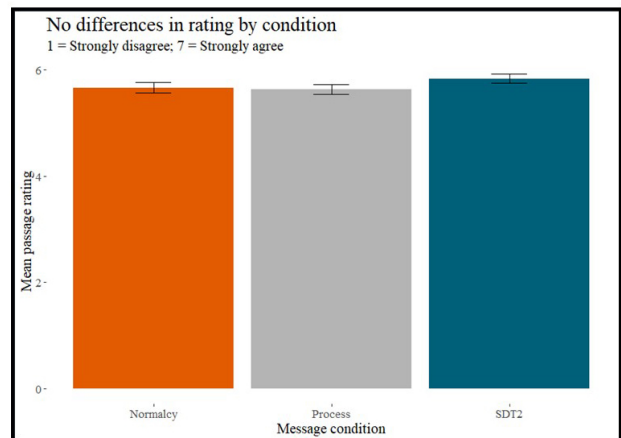
Background. The COVID-19 pandemic has brought vaccination to the forefront of discourse on public health. The rapid speed of COVID-19 vaccine development, utilization of novel technology, and an atmosphere of politicized misinformation have created a perfect storm for vaccine hesitancy. As early adopters of vaccination, HCWs set an example for the general population; as trusted sources of medical information, they educate and inform. However, comparatively little work has investigated HCWs' attitudes toward vaccination and how those attitudes drive their recommendation behavior.

Methods. We surveyed hospital employees about their personal reasons for hesitancy and beliefs about patient hesitancies and randomly assigned them to see one of three messages aimed at increasing vaccine confidence. Message themes included an appeal to return to normal life (Normalcy), a risk comparison between vaccinating or not (SDT), and an explanation of the speed of safe and effective vaccine development (Process).

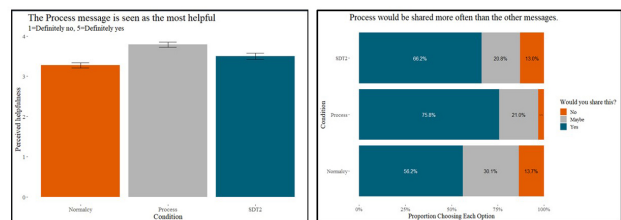
Results. Of the 674 NC hospital employees who completed our survey in February 2021, 98% had been offered the COVID-19 vaccine, and 80% had already accepted. For the 20% who had not received the vaccine, the top reasons for hesitancy

involved the speed of development and testing, and concerns of vaccine safety and effectiveness. We also found differences in susceptibility to misinformation and vaccine hesitancy across political affiliation, which was higher in Republicans compared to Democrats. HCWs were generally very comfortable recommending the COVID-19 vaccine to patients and supported the idea of sharing the message they read. Although the risk comparison message was most trusted personally, the process message was rated as both the most helpful to patients and the most likely to be shared with them (see Figure 1). This suggests that what is most appealing on a personal level is not necessarily what a HCW would recommend to their patients.

Rating of personal opinions of the passages.



On a scale from 1 to 7 with 1 = Strongly Disagree and 7 = Strongly Agree. This chart shows the average message ratings across the board when answering whether they thought the passages were understandable, helpful, correct, believable, and trustworthy. (Error bars are 95% CI) There was no significant difference across the messages. The Process message is seen as most helpful and is most likely to be shared with patient than the other messages



On left, the average answer on a scale from 1 to 5 for "Do you think the passage you just read would help your patients feel more comfortable about getting the vaccine?" and on right, the average answer for "Would you share this passage with your patients?"

Conclusion. HCWs' high uptake and minimal hesitancy in recommending the COVID-19 vaccine is encouraging and merits further exploration for how to increase confidence in HCW who are hesitant to discuss and recommend vaccines to patients, as several highlighted the importance of respecting patient autonomy.

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581. COVID-19 Vaccine Perceptions in Adults from Greater Nashville Tennessee

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Session: P-25. COVID-19 Vaccines

Background. In December 2020, SARS-CoV-2 vaccines were made available to healthcare workers and soon thereafter offered to the general public according to age and risk of severe illness. Despite widespread access, vaccination rates vary by region, with Tennessee ranking lower than the national average. Therefore, we aimed to survey adults in greater Nashville, TN regarding SARS-CoV-2 vaccine perceptions.

Methods. We conducted a cross-sectional study of an ongoing longitudinal cohort of individuals with confirmed and/or suspected SARS-CoV-2 infection and their household contacts with enrollment onset in March 2020. For this analysis, individuals were included if they were ≥ 18 years and available for a one-year follow-up visit. At the one-year visit individuals completed a survey about vaccine preferences, beliefs and